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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,684	11/02/2006	Morey Kraus	07588/020002	4507

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EXAMINER	
BARNHART, LORA ELIZABETH	
ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
01/27/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/583,684	KRAUS ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7 and 48-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7 and 48-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/15/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments

Applicant's amendments filed 11/15/10 to claims 1 and 7 have been entered. Claims 2-6 and 8-47 have been canceled. Claims 48-54 have been added. Claims 1, 7, and 48-54 remain pending in the current application and are being considered on their merits. References not included with this Office action can be found in a prior action. Any rejections of record not particularly addressed below are withdrawn in light of the claim amendments and applicant's comments.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7, and 48-54 are/remain rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating any diabetes by administering the pluripotent cell described in claim 1 using any of the means recited in claim 52. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in

the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

Applicants amended claim 1 to limit the disease to diabetes and the administered cell to an umbilical cord blood (UCB) or placental blood cell per se (i.e., removing a limitation that permitted administering "progeny cells"). Claim 1 is currently drawn to a method of treating diabetes by administering a UCB or placental blood cell expressing particular markers to a patient in need thereof; in claims 48-53, the manner of administration is particularly described. Claim 54 requires administering "an agent that induces said cell to differentiate into a pancreatic islet cell *in vivo*." These elements will be addressed in turn.

The specification is not enabling for treating diabetes by administering CD34- UCB or placental blood cells.

Treatment of diabetes by administration of UCB or placental blood stem cells was unpredictable at the time of the invention, i.e. 12/19/03. After a diligent search, the examiner located only one relevant prior art reference in which UCB was administered to NOD-SCID (nonobese, diabetic, severe combined immunodeficiency) mice. Lewis et al., 2001, *Blood* 97: 3441-49 (reference U). Lewis, however, administered CD34-expressing UCB cells, while the cells administered in instant claim 1 do not express CD34. (Lewis at 3442.) Furthermore, Lewis observed only that the CD34+ UCB cells

engrafted, not that the mice's diabetic condition was treated. (Lewis at 3446.) Lewis does not suggest administering the CD34- cells recited in claim 1.

Years after the invention, skilled artisans still viewed the treatment of diabetes with stem cells as an unsolved problem. Haller et al. (2008, *Experimental Hematology* 36: 710-15; on 11/15/10 IDS) investigated infusions of autologous UCB for treating type I diabetes . Pages 712-13. Haller characterized the data from this study as "preliminary" and even "flawed," concluding that significant additional work would be required before stem cell therapy for diabetes becomes a reality. Page 714. Haller's statement that "the only means allowing for the reversal of [type I diabetes] involves whole pancreas or islet cell transplantation in association with non-specific immunosuppressive therapy" at page 711, column 1, is noteworthy, since it indicates that years after the invention, stem cell therapy was not an accepted treatment for diabetes and that skilled artisans would have considered such therapy to be unpredictable.

As discussed in the previous Office action, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification needs more detail as to how to make and use the invention in order to be enabling. See M.P.E.P. § 2164.03. The instant specification provides no particular guidance for treating each and every pancreatic disease with any cell or active agent. The working examples include none in which any cells are administered to any patient with a pancreatic disease. The only possibly relevant examples, Examples 6-8 at pages 26-27 are limited to what appear to be prophetic administrations of stem cells into hepatectomized mice or preimmune sheep. Neither of these prophetic examples discusses treatment of diabetes

or any other pancreatic or hormonal condition. The specification includes no examples in which the cells recited in the claims differentiate into any pancreatic cell, either *in vitro* or *in vivo*. Indeed, the specification mentions diabetes only in passing, in a list of "non-limiting examples of hepaticopancreatic disorders." Page 16, lines 18-20. The disclosure provides insufficient guidance to practice the invention, taken in view of its unpredictable nature at the time of filing.

The specification is not enabling for treating diabetes by administering cells via all of the routes in claim 52.

Claim 52 allows that the administration step in the diabetes treatment method of claim 1 may be "intracoronary, retrograde venous, intraventricular, intracerebroventricular, cerebrospinal, [or] intracranial," which is puzzling given the location of the pancreas within the abdomen. The examiner is unable to locate any teachings that would have given the skilled artisan a reasonable expectation in 2003 (or any time) that administering stem cells into the ventricles of the brain, within the cerebrospinal fluid, or into the heart would have any effect on the pancreas. The administration sites in claim 52 have no clear link to the treatment of diabetes. Again, the specification mentions the sites in claim 52 only in passing, in a list of exemplary administration routes for general infusion of stem cells. Page 22, lines 11-15. The paragraph that lists these routes makes no mention of diabetes, which is the only disorder treated by the current claims.

Regarding the enablement rejection of record, which addressed claims with a very different scope, applicants allege that the specification teaches how to make the

cells required for the claimed method. (Reply at 7.) Applicant refers to 2008 and 2009 experiments performed by Haller in support of an enabling disclosure. (Reply at 8.) These arguments have been fully considered, but they are not persuasive of error.

The examiner has not alleged that the specification does not teach how to make the claimed cells. At issue here is the degree of success the skilled artisan could reasonably have expected at the time of the invention in carrying out the claimed invention. Applicant's reliance on Haller's studies is unimpressive. The examiner's position is that the 2008 Haller reference is, at best, preliminary data; more to the point, however, both Haller publications are completely irrelevant to the state of the art at the time of filing, i.e. 2003. See M.P.E.P. § 2164.05(a) ("[A] later dated publication cannot supplement an insufficient disclosure in a prior dated application to make it enabling. . . ."); *Ariad Pharms. Co. v. Eli Lilly & Co.*, 94 U.S.P.Q.2d 1161, 1173 (Fed. Cir. 2010) (en banc) ("Patents are not awarded for academic theories, no matter how groundbreaking or necessary to the later patentable inventions of others."). The fact that Haller carried out the claimed invention six or seven years after the filing date cannot make the instant disclosure enabling.

Claim 54 is also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 54 requires administering, in addition to

the cells in claim 1, "an agent that induces said cell to differentiate into a pancreatic islet cell *in vivo*." There is insufficient disclosure to demonstrate that applicants possessed even one such agent, much less all agents with the required function. Such "reach-through" claims were addressed by the Federal Circuit in *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 920-23, 69 USPQ2d 1886 (Fed. Cir. 2004). See M.P.E.P. § 2163.

Regarding the written description requirement in reach-through situations, the CAFC wrote, "While it is true that this court and its predecessor have repeatedly held that claimed subject matter 'need not be described *in haec verba*' in the specification to satisfy the written description requirement…it is also true that the requirement must still be met in some way so as to 'describe the claimed invention so that one skilled in the art can recognize what is claimed.' *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 963 at 968 (63 USPQ2d 1609) (Fed. Cir. 2002). We have further explained that:

> [T]he appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. … A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its function of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice. [*Regents of the Univ. of Cal. v.] Eli Lilly [& Co., Inc.*], 119 F.3d [1559,] 1568 [43 USPQ2d 1398] [(Fed. Cir. 1997) ("Lilly")] … . The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *Id.*

Enzo, 323 F.3d at 968. Similarly, for example, in the nineteenth century, use of the word "automobile" would not have sufficed to describe a newly invented automobile; an inventor would need to describe what an automobile is, *viz.*, a chassis, an engine, seats, wheels on axles, etc. Thus, generalized language may not suffice if it does not convey the detailed identity of an invention." *Rochester*, 358 F.3d at 1892.

In sum, the instant specification does not provide any guidance that would steer the skilled practitioner toward any agent that can be used to carry out the claimed method and has not provided evidence that any such agents were otherwise within the knowledge of a person of ordinary skill in the art at the relevant time. All that is suggested is trial-and-error *in vitro* experimentation, a suggestion unaccompanied by any information tending to show that such trial and error would be a fruitful search for an agent with the required *in vivo* effect. Page 4, lines 4-17. The only discussion of an agent being administered *in vivo* is at page 12, lines 7-9, which merely recites the language of claim 54 and suggests administering such an agent. The disclosure is broad and vague and does not define any particular agent that would, upon administration, induce infused stem cells to differentiate into pancreatic islet cells within the body. Applicant has provided no argument or evidence tending to demonstrate possession, and the specification fails to identify by structure even one agent that has the required function. Claim 54 fails the description requirement.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7, and 48-54 are/remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to “A method of treating diabetes comprising administering to a patient in need thereof a cell . . .,” which is confusing because it is not clear whether “thereof” refers to “diabetes,” the “method” itself, the “cell,” or some other element.

Clarification is required. Because claims 7 and 48-54 depend from indefinite claim 1 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 7 requires that the method comprise "administering said cell to effect regeneration or pancreatic islet cells," but it is not clear whether this regeneration actually occurs as part of the method or whether this limitation merely recites one possible intended use of the administration step. Applicant alleges that the amendment to the claims overcomes the rejection and that the action may be "direct" or "indirect." (Reply at 6-7.) These arguments have been fully considered, but they are not persuasive of error. The question arises not because of the scope of the effect, but because the examiner cannot deduce whether this effect is an inherent effect of the method step in claim 1 (in which case claim 7 is redundant) or whether some additional, unrecited step or condition is required to produce the effect (in which case claim 7 is incomplete and must be amended to describe the essential step or condition necessary to yield the result). Clarification is required.

Claim 54 refers to "an agent that induces said cell to differentiate into a pancreatic islet cell *in vivo*," which is confusing because it defines the agent wholly functionally. While describing a product in terms of its function is not itself improper (see *In re Swinehart*, 439 F.2d 210, 169USPQ 226 (CCPA 1971)), claims directed to a product should be distinguished from the prior art product in terms of structure rather than function; this point was recently revisited. "When a claim limitation is defined in purely functional terms, the task of determining whether that limitation is sufficiently

definite is a difficult one that is highly dependent on context (e.g., the disclosure in the specification and the knowledge of a person of ordinary skill in the relevant art area). We note that the patent drafter is in the best position to resolve the ambiguity in the patent claims, and it is highly desirable that patent examiners demand that applicants do so in appropriate circumstances so that the patent can be amended during prosecution rather than attempting to resolve the ambiguity in litigation." *Halliburton Energy Services, Inc. v. M-I LLC*, 85 USPQ2d 1654, 1663 (Fed. Cir. 2008). Such ambiguity could be resolved in a few ways, for example by providing a quantitative metric for the property, or a formula for calculating the claimed functional property along with examples and counterexamples of products with that property. While functional claiming is authorized by 35 U.S.C. § 112, sixth paragraph, that statute was enacted specifically to preclude overly broad claims that effectively purport to cover any and all limitations, so long as they perform the required functions. Specifically, claims that are ambiguous as to boundaries for functional limitations may be indefinite and do not distinguish the claimed product over the prior art. Here, claim 54 appears to be an attempt to embrace all agents that are at some time in the future found to have the desired activity. The scope of these agents was unknown at the time of the invention and, therefore, indefinite. Clarification is required.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is (571)272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lora E Barnhart/
Primary Examiner, Art Unit 1651